- and / or the presence of the more soluble substance lowers the average elastic energy of the membrane-like coating to a value at least 5 times lower, more preferably at least 10 times lower and most preferably more than 10 times lower, than the average elastic energy of red blood cells or of phospholipid bilayers with fluid aliphatic chains,
- said penetrants being able to transport agents through the pores of said barrier or to enable agent permeation through the pores of said barrier after penetrants have entered the pores,
- selecting a dose amount of said penetrants to be applied on a predetermined area of said barrier to control the flux of said penetrants across said barrier, and
- applying the selected dose amount of said formulation containing said penetrants onto said area of said porous barrier.

Preferably the flux of penetrants across said barrier is increased by enlarging the applied dose amount of said penetrants.

It then is preferred if the pH of the formulation is between 3 and 10, more preferably is between 4 and 9, and most preferably is between 5 and 8.

According to another preferred feature of the present invention the formulation containing the penentrants comprises:

- at least one thickening agent in an amount to increase the formulation viscosity to maximally 5 kN s/m$^2$, more preferably up to 1 kN s/m$^2$, and most preferably up to 0.2 kN s/m$^2$, so that formulation spreading-over, and drug retention at the application area is enabled,
- and / or at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months, more preferably to less than 100 % per 12 months and most preferably to less than 50 % per 12 months

250 nm, even more preferably between 50 nm and 200 nm and particularly preferably between 60 nm and 150 nm.

It is another preferred feature of the present invention that the total dry weight of droplets in a formulation is 0.01 weight-% (w-%) to 40 w-% of total formulation mass, more preferably is between 0.1 w-% and 30 w-%, and most preferably is between 0,5 w-% and 20 w-%.

According to the present invention is is preferred if at least one edge-active substance or surfactant and/or at least one amphiphilic substance, and / or at least one hydrophilic fluid and the agent are mixed, if required separately, to form a solution, the resulting (partial) mixtures or solutions are then combined subsequently to induce, preferably by action of mechanical energy such as shaking, stirring, vibrations, homogenisation, ultrasonication, shearing, freezing and thawing, or filtration using convenient driving pressure, the formation of penetrants that associate with and / or incorporate the agent

Preferrably this amphiphilic substances are dissolved in volatile solvents, such as alcohols, especially ethanol, or in other pharmaceutically acceptable organic solvents, such as ethanol, 1- and 2-propanol, benzyl alcohol, propylene glycol, polyethylene glycol (molecular weight: 200-400 D) or glycerol, other pharmaceutically acceptable organic solvents, such as undercooled gas, especially supercritical $CO_2$, which are then removed, especially by evaporation or dilution, prior to making the final preparation.

preferably is between 4 and 9, and most preferably is between 5 and 8.

In this aspect of the invention, it then is preferred if the formulation comprises:

- at least one thickening agent in an amount to increase the formulation viscosity to maximally 5 kN s/m$^2$, more preferably up to 1 kN s/m$^2$, and most preferably up to 0.2 kN s/m$^2$, so that formulation spreading-over, and drug retention at the application area is enabled,
- and / or at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months, more preferably to less than 100 % per 12 months and most preferably to less than 50 % per 12 months
- and / or at least one microbicide in an amount that reduces the bacterial count of 1 million germs added per g of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 4 days.

Said at least one microbicide then preferably is added in an amount that reduces the bacterial count of 1 million germs added per g of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 3 days, and more preferably after a period of 1 day.

Said thickening agent preferrably is selected from the class of pharmaceutically acceptable hydrophilic polymers, such as partially etherified cellulose derivatives, like carboxymethyl-, hydroxyethyl-, hydroxypropyl-, hydroxypropylmethyl- or methyl-cellulose; completely synthetic hydrophilic polymers such as polyacrylates , polymethacrylates, poly(hydroxyethyl)-, poly(hydroxypropyl)-, poly(hydroxypropylmethyl)methacrylates, polyacrylonitriles, methallyl-

phosphorylglycerol, or -phosphorylserine, n-acyl-, e.g. lauryl or oleoyl-glycero-phosphatidic acid, -phosphorylglycorol, or -phosphorylserine, n-tetradecyl-glycero-phosphatidic acid, -phosphorylglycerol, or - phosphorylserine, a corresponding palmitoeloyl-, elaidoyl-, vaccenyl-lysophospholipid or a corresponding short-chain phospholipid, or else a surface-active polypeptide.

The average diameter of the penetrant preferrably is between 30 nm and 500 nm, more preferably between 40 nm and 250 nm, even more preferably between 50 nm and 200 nm and particularly preferably between 60 nm and 150 nm.

The total dry weight of droplets in a formulation is then preferrably chosen to range from 0.01 weight-% (w-%) to 40 w-% of total formulation mass, more preferably is between 0.1 w-% and 30 w-%, and most preferably is between 0,5 w-% and 20 w-%.

Preferably at least one edge-active substance or surfactant and/or at least one amphiphilic substance, and / or at least one hydrophilic fluid and the agent are mixed, if required separately, to form a solution, the resulting (partial) mixtures or solutions are then combined subsequently to induce, preferably by action of mechanical energy such as shaking, stirring, vibrations, homogenisation, ultrasonication, shearing, freezing and thawing, or filtration using convenient driving pressure, the formation of penetrants that associate with and / or incorporate the agent